MEETING BRIEFS

Neuroscience's Meeting of the Minds in Washington

WASHINGTON, D.C.—Nearly 25,000 neuroscientists gathered last week at the Washington Convention Center and in sessions at nearby hotels for what Society for Neuroscience president Pasco Rakic dubbed "the largest gathering of neuroscientists in the history of the world." Here are a few highlights from the meeting.

New View of Spinal Cord Injury

Every year, spinal cord injuries leave up to 15,000 people in the United States partly or totally paralyzed. The only treatment now is the steroid drug methylprednisolone, which can curb some of the damage if given within 8 hours of the injury. But many spinal cord patients are still left devastated. Research presented in Washington suggests a new strategy for reducing that toll.

In work done with rats, four teams, led by Michael Beattie and Jackie Bresnahan at

M. BEATTIE AND J. BRESNAHAN

Slow death. Spinal cord cells die from apoptosis (arrow) for up to 3 weeks after injury.

Ohio State University College of Medicine in Columbus, Dennis Choi of Washington University in St. Louis, Russ Nockels and Michael Chopp at Henry Ford Hospital in Detroit, and Barry Fetoff of the Veterans' Administration Medical Center in Kansas City, Kansas, focused on a wave of spinal-cell death that continues for up to 3 weeks after the injury. They found that the cells die not from damage done by the blow itself, but from programmed cell suicide (apoptosis). And they report hints that stopping that apoptosis could reduce the extent of paralysis.

Researchers had known that much of the cell death in spinal cord injury is delayed but didn't know why. But the four groups now provide "definite evidence" that apoptosis is key to that secondary injury, says Andrew Blight, who studies spinal cord injury at the University of North Carolina. The research also suggests "a reasonable chance," he says, that apoptosis blockers being developed for treatment of other conditions may help limit spinal cord injuries.

All four teams used a rat model designed by Wise Young at New York University to reflect the most common kind of spinal cord injury in humans, in which the cord is not severed but is deeply bruised from a fall or a blow. The rat studies show that the initial injury destroys some of the neuronal axons running down the cord. But those that survive the initial blow aren't out of danger—damage and cell death continue to spread following the injury. Among the cells that die are oligodendrocytes, nonneuronal cells that wrap axons in insulating layers of myelin. Without the oligodendrocytes, axons lose their myelin and are unable to conduct impulses. Until recently, says Blight, some researchers thought that all this additional damage was the result of the slow death of cells already injured by the original blow.

Now, it seems that it's not. Examining the spinal cords of rats at various times after injury, the researchers found signs that the cells were dying not from physical injury, but from the orderly process of apoptosis, in which cells chop up their chromosomes while keeping their membranes intact. These findings aren't confined to rats; Bresnahan found similar signs of apoptosis in damaged monkey spinal cord as well.

Many of the dying cells are the myelin-producing oligodendrocytes. Because oligodendrocytes seem to need contact with healthy axons to survive, Beattie suggests that the dying back of some of the axons during the original injury could be the trigger causing the oligodendrocytes to die; their death could then cause further axon demyelination.

Because the apoptosis continues for 3 weeks following spinal cord injury in rats, it may open a longer window of opportunity for therapies, says Nockels. Indeed, both the St. Louis and Detroit teams have evidence in rats that such interventions may work. Choi's group treated injured rats with the protein synthesis blocker cycloheximide, which prevents apoptosis, and got a 50% improvement in the animals' ability to use their hind legs after the injury. "This gives a glimpse of the potential functional benefit," says Choi. However, cycloheximide is too toxic for human use, so [illegible] must await other apoptosis blockers now under development.

Neurotrophic factors, which protect neurons and other cells from apoptotic death, may be an alternative. Nockels's team implanted cells making nerve growth factor or brain-derived neurotrophic factor directly into injured spinal cords, and found that the animals recovered faster than controls. They haven't yet shown whether this is due to the prevention of apoptosis, however.

Nor do researchers know whether an antiapoptotic drug would add to the effects of methylprednisolone, because its mode of action is uncertain. "It would be great to test the two together," says Blight. But the new cell-suicide findings are encouraging, say the researchers. Someday, predicts Fetoff, "the acute treatment for spinal cord injury ... is going to be a syringe."

—Marcia Barinaga

Leptin: A Trigger for Puberty?

The protein famous for making fat mice thin, in part by signaling their brains that they've eaten enough, also seems to regulate an entirely different kind of appetite: the sex drive. Endocrinologist Jeffrey Flier of the Beth Israel Deaconess Medical Center in Boston presented evidence here that leptin—a protein that has sparked enormous interest as a possible obesity drug since its discovery 2 years ago—helps regulate sex hormone production. Indeed, it may even be the trigger for the onset of puberty.

If so, the discovery would help explain a variety of observations made over the years relating body fat content to sexual behavior and fertility. Scientists have known for years, for example, that ballet dancers, marathon runners, and others with low body fat have disrupted reproductive systems, as do people who are starving. Women stop ovulating, and testosterone levels fall in men. Because leptin is made and secreted by fat cells, the drop in production that occurs in very lean or starving people might account for these changes—an idea described as "very satisfying" by Rose Frisch, a population scientist at the Harvard School of Public Health in Boston who has studied the connection between fat and fertility for several decades.

The work also adds to growing evidence that leptin's function is not only to prevent weight gain, but also to help the body conserve energy during a famine by regulating the complex neuroendocrine system that governs metabolism and the energy-expensive reproductive system, says Arthur Campfield, who studies metabolic diseases at Hoffmann-La Roche in Nutley, New Jersey, and who